

**IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION**

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL No. 2327
THIS DOCUMENT RELATES TO:	JOSEPH R. GOODWIN U.S. DISTRICT JUDGE
WAVE 3 CASES	

**PLAINTIFFS' RESPONSE TO DEFENDANT ETHICON'S MOTION TO EXCLUDE
THE OPINIONS AND TESTIMONY OF VLADIMIR IAKOVLEV, M.D**

Plaintiffs in the above-captioned cases respectfully submit this supplemental Memorandum of Law in Opposition to Defendant, Ethicon's Motion to Exclude the Opinions and Testimony of Vladimir Iakovlev, M.D. and Memorandum in support thereof ("Def. Br.").¹

This Court entered its *Daubert* order regarding Ethicon's motion to exclude certain of Dr. Iakovlev's opinions on September 1, 2016. *In re Ethicon, Inc. Pelvic Repair Sys. Prods. Liability Litig.*, No. 2:12-MD-02327, Dkt. 2710 (S.D. W. Va. Sep. 1, 2016). Plaintiffs hereby respond to two discreet Daubert issues addressed in the parties' briefing as well as the Court's *Daubert* order: Mesh folding/deformation and Complications.

I. Dr. Iakovlev's Opinions in this case

As this Court has previously noted, Dr. Iakovlev is a highly qualified clinical pathologist whose practice involves the examination of 5,000 cases annually (Dr. Iakovlev's Expert Report is attached hereto as Exhibit A.) Dr. Iakovlev has reviewed transvaginal mesh samples in

¹ Ethicon adopted its Motion to Exclude the Opinions and Testimony of Dr. Vladimir Iakovlev filed in Wave 1 [*In re Ethicon, Inc. Pelvic Repair Sys. Prods. Liability Litig.*, No. 2:12-MD-02327, Dkt. 2850 (S.D. W. Va. Sep. 19, 2016)]. Plaintiffs hereby incorporate by reference their Wave 1 Response to Defendant Ethicon's Motion to Exclude the Opinions and Testimony of Dr. Vladimir Iakovlev. This brief addresses two issues on which Plaintiffs would respectfully ask the Court to reconsider its prior rulings.

connection with his work as a pathologist at St. Michael's Hospital. Ex. A at 2. In addition, Dr. Iakovlev has reviewed mesh samples provided to him in litigation.

The testimony and opinions that Dr. Iakovlev offers in this case are substantially the same as those he has previously presented in Court in five separate pelvic mesh trials.² (Dr. Iakovlev's deposition, dated September 14, 2015, is attached hereto as Exhibit B."). Each of these opinions is well supported with citations to the medical and scientific literature, and each is supported by Dr. Iakovlev's experience as an anatomical pathologist reviewing the explanted meshes of the Wave 1-3 Plaintiffs. He conducted a pathologic review of the available materials "in the same manner that [he] would analyze routine diagnostic specimens according to the standard operating procedures of an accredited diagnostic laboratory." Ex. A at 2. In reaching his opinions in this case, Dr. Iakovlev stated that:

For the opinions and figures in this report, I have relied on my findings in the explant specimens, including those transvaginal mesh devices manufactured by Ethicon. In addition, I have also relied on data available in peer-reviewed publications, including my own peer-reviewed publications. A short review of the published literature is provided below:³

Ex. A at 5. He utilized the same "methodology that [he] has previously used when [he] testified in the . . . southern district of West Virginia . . . and in other courts where [he] has been allowed to testify at trial." Ex. B. at 298:14-299:4. This same methodology has been an acceptable part of clinical pathological practice for over 100 years.

² *Deborah Barba v. Boston Scientific Corp.*, State of Delaware, Superior Court, C.A. No. N11C-08-050 MMJ (May 19, 2015); *Dianne Bellew v. Ethicon, Inc.*, The United States District Court, Southern District of West Virginia, MDL NO. 2327; 2:12-cv-22473 Charleston, WV, USA (March 5, 2015); *Amal Eghnayem et al. v. Boston Scientific Corp.*, The United States District Court, Southern District of West Virginia, MDL NO. 2326; 2:13-cv-07965 Miami, Florida, USA (Nov. 6, 2014); *Maria Cardenas v. Boston Scientific Corp.*, Commonwealth of Massachusetts, Superior Court MICV2012-02912, Boston, Massachusetts, USA (August 18, 2014); and, *Jennifer Ramirez v. Ethicon Inc.*, State of Texas, District Court, 2012-CI-18690, Bexar County (April 19, 2016)(by *de bene esse*)

³ *Eghnayem v. Boston Sci. Corp.*, 57 F. Supp. 3d 658, 669 (S.D.W. Va. 2014).

I. LEGAL STANDARD

Plaintiffs incorporate by reference the standard of review for *Daubert* motions articulated by the Court in *Edwards v. Ethicon, Inc.*, No. 2:12-CV-09972, 2014 WL 3361923, at **1-3 (S.D.W. Va. July 8, 2014). As this Court has previously concluded,

I “need not determine that the proffered expert testimony is irrefutable or certainly correct” — “[a]s with all other admissible evidence, expert testimony is subject to testing by ‘[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof.’” . . . “[t]he inquiry to be undertaken by the district court is ‘a flexible one’ focusing on the ‘principles and methodology’ employed by the expert, not on the conclusions reached.”⁷

II. ARGUMENT

A. Mesh Folding and Deformation

The concept of “mesh contraction” (used interchangeably in the scientific literature, in the medical records of mesh plaintiffs, in the internal company documents, as well as in countless corporate depositions mesh “shrinkage,” mesh “bunching,” mesh “deformation,” mesh “ridging,” mesh “curling,” mesh “banding,” and mesh “folding,” just to name a few) is well known to this Court through numerous trials and motions, and is equally well known by scientists and surgeons in the world of surgical mesh. Dr. Iakovlev cited to many of these in his Wave reports. (Ex. A at 12-13; 113) It is a whopping understatement to say that Dr. Iakovlev is not alone in his knowledge and opinions regarding the fact—not theory, but *fact*—that when the wound around the surgical site begins to heal in the post-operative period, like any wound, it contracts. And when mesh is laid flat within that wound during the surgery, as it most necessarily and intentionally is, during the post-operative period, as the wound heals and contracts, the mesh “shrinks” and becomes bunched and folded or otherwise deformed. (Ex A at 6-7) The only question becomes, to what extent in any given patient has the mesh contracted/bunched/folded/deformed; and the only way to determine that is to analyze it upon explant—grossly and microscopically. That is what Dr.

Iakovlev has done hundreds of times in both his clinical practice at St. Michael's and in the context of this litigation. And he has done so following the same methodology as is done by him and other pathologists around the world every day—review the patient's clinical history and the reason for the surgery; examine the pathological specimen grossly (with the human eye); examine the pathological specimen microscopically (with histological staining under the microscope); and then analyze what is seen and arrive at a pathological differential diagnosis taking the patient's medical records, the gross findings, the microscopic findings, the pathologist's background, training and experience, and all relevant peer-reviewed literature and learned treatises into account. His methodology is outlined in the various case-specific reports that he has provided throughout this litigation. (Dr. Iakovlev's Case-Specific Expert Report is attached hereto as Exhibit C.)

In its *Daubert* ruling, this Court held that “Dr. Iakovlev's opinions on folding and curling are **EXCLUDED** *to the extent they rely solely on his personal analysis of pathology slides*, and Ethicon's Motion is **GRANTED** on this point.” (emphasis added). However, Dr. Iakovlev's opinions are by no means based solely on his analysis of the pathology slides. His opinions were also based on:

- Peer-reviewed literature set forth in his report and on his reliance list to that report describing mesh folding and deformation *in vivo* in both pathological slides and gross pathological examinations;⁴

⁴ Klosterhalfen, B. & Klinge, U, "Retrieval study at 623 human mesh explants made of polypropylene--impact of mesh class and indication for mesh removal on tissue reaction," *J Biomed Mater Res B Appl Biomater*, vol. 101, pp. 1393-9, 2013 (Ex. A at 126).; Elliott, M. & Juler, G, "Comparison of Marlex mesh and microporous teflon sheets when used for hernia repair in the experimental animal," *Am J Surg*, vol. 137, pp. 342-4, 1979. (Ex. A at 12, 120); García-Ureña MA, Vega Ruiz V, Díaz Godoy A, Báez Perea JM, Marín Gómez LM, Carnero Hernández FJ, Velasco García MA, "Differences in polypropylene shrinkage depending on mesh position in an experimental study," *Am J Surg*, vol. 193, pp. 538-42, 2007. (Ex. A at 121); Klinge U, Klosterhalfen B, Mueller M, Ottinger AP, Schumpelick V, "Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs," *Eur J Surg*, vol. 164, pp. 965-969, 1998 (Ex A. at 12, 126); Iakovlev V., E. Carey, J, Steege, "Pathology of Explanted Transvaginal Meshes,"

- Well-established knowledge from urogynecological and abdominal surgeons in the peer-reviewed literature describing *in vivo* mesh folding and deformation in both pelvic floor and hernia repair;⁵
- Peer-reviewed literature describing mesh “waviness”, folding and other types of deformation by the use of ultrasound *in vivo*;⁶
- Intraoperative reports of pelvic mesh excisions. Examples from some of the Wave 1-3 cases included:
 - Ms. Barbara Vignos-Ware: 11/24/2010. Cleveland Clinic. Dr. Walters. Operative report of mesh excision: “Mesh was bunched up in the middle and twisted, was difficult to delineate borders of the mesh.”
 - Ms. Virginia White: 03/18/2009. Washington Regional Medical Center. Operative report of mesh excision: “The mesh pulled together in one thick band.”
 - Ms. Diana Allen: 09/29/2011. Indiana University Health. Dr. Hale. Operative report of mesh excision: “It appeared as though the mesh had folded over on itself and contracted in these locations.”

International Journal of Medical, Health, Pharmaceutical and Biomedical Engineering, vol. 8, no. 9, pp. 510-13, 2014 (Ex. A at 7, 8, 123); Bendavid R, Lou W, Koch A, Iakovlev V, "Mesh-Related SIN Syndrome. A Surreptitious Irreversible Neuralgia and Its Morphologic Background in the Etiology of Post-Herniorrhaphy Pain," *Int J Clin Med*, vol. 5, pp. 799-810, 2014 (Ex. A at 7, 11, 115).

⁵ Haylen, B. et al., "An International Urogynecological Association (IUGA)/International Continence Society (ICS) Joint Terminology and Classification of the Complications Related Directly to the Insertion of Prosthesis (Meshes, Implants, Tapes) and Grafts in Female Pelvic Flo," *Neurourol Urodynam*, vol. 30, pp. 2-12, 2011 (Ex. A at 122); Barnes MG. , "Irritable bowel syndrome: a "mesh" of a situation," *J Am Board Fam Med*, vol. 25, no. 1, pp. 120-3, 2012 (Ex. A at 6-7, 11-12, 66, 141)); Tunn R, Picot A, Marschke J, Gauruder-Burmester A, "Sonomorphological evaluation of polypropylene mesh implants after vaginal mesh repair in women with cystocele or rectocele," *Ultrasound Obstet Gynecol*, vol. 29, no. 4, pp. 449-52, 2007 (Ex. A at 143).

⁶ Svabík, K. et al. , "Ultrasound appearances after mesh implantation--evidence of mesh contraction or folding?," *Int Urogynecol J*, vol. 22, pp. 529-33, 2011 (Ex A. at 12, 140); Kumar, V., Abbas, A., Fausto, N. & Aster, J , Robbins and Cotran Pathological Basis of Disease, 8th Edition, Elsevier, Imprint: W.B. Saunders, 2010 (Ex. A at 136).

As set forth in the numerous publications cited herein, and in Dr. Iakovlev's Wave reports, the process of wound contraction and mesh shrinking/bunching/folding/etc. is a progressive phenomenon that occurs *in vivo* after the mesh is implanted. Once the mesh is explanted, Dr. Iakovlev proceeds with his normal pathological analysis and differential diagnosis —review of records, gross examination (see, feel and measure), and then slides are cut to be viewed microscopically. (Ex. C) His gross and microscopic findings are then correlated to the medical history and reason for explantation. Each of the meshes in Waves 1-3 have been examined grossly by Dr. Iakovlev (when received in formalin) and then cut to examine their inner configuration before they are processed for microscopic examination (*See* Exs. D-H, attached hereto as examples of gross and histologic examples from Wave cases showing gross and microscopic depictions of mesh deformation/bunching/etc.) The clinical descriptions, gross examination and histological examinations of mesh deformation and other findings have been correlated in each of Dr. Iakovlev's Wave case-specific reports utilizing uniform, accepted, well-established pathological methodology done by pathologists in the field.

In summary, Dr. Iakovlev's opinions regarding mesh deformation/folding/contraction/curling/etc. are based on sound methodology employed by other pathologists in the field and are well supported by numerous scientists and surgeons in the peer-reviewed literature and indeed, by his own pathological analysis of hundreds of mesh explants. As such, plaintiffs respectfully request that the Court deny Ethicon's motion to exclude his opinions regarding mesh deformation *in vivo*.

B. Complications

In its recent *Daubert* order, the Court ruled that “[t]o the extent that Dr. Iakovlev offers complications opinions based on his examination of explanted mesh samples without the use of a control sample, his complications opinions are EXCLUDED.” *In re Ethicon, Inc. Pelvic Repair Sys. Prods. Liability Litig.*, No. 2:12-MD-02327, Dkt. 2710 at *9 (S.D. W. Va. Sep. 1, 2016). The Court reasoned that “[w]ithout a proper control, Dr. Iakovlev’s opinions correlating specific complications with samples of explanted mesh products do not provide a sufficiently reliable methodology.” *Id.* This holding begs the question: “What constitutes a ‘proper control’ in the context of a pathologist employing well-accepted, standard methodology in arriving at a pathological diagnosis of a particular complication in any given patient?” As the United States Supreme Court held in *Kumho Tire*, the crux of the *Daubert* inquiry “is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.” *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). Given this holding, a review of what constitutes accepted methodology by pathologists in the field in arriving at a pathological diagnosis based on the practitioner’s clinical-pathological correlation in a given case is critical to the Court’s decision in this regard.

In his Wave expert reports, Dr. Iakovlev relies upon one of the most recognized and well-regarded pathology treatises, *Pathological Basis of Disease*, by Robbins and Cotran.⁷ This textbook is so well regarded that it is used as a guide for the pathology licensing exams. (**Affidavit of Vladimir Iakovlev, MD attached as Ex. I, para 1**) In its introductory page, it sets forth the basics, the “Pathology 101,” of what pathologists do in their daily work:

⁷ Robbins and Cotran *Pathological Basis of Disease*, 8th Edition, Elsevier, Imprint: W.B. Saunders, 2010. (Ex. A at 6, 127)

“By the use of molecular, microbiologic, immunologic, and morphologic techniques, pathology attempts to explain the whys and wherefores of the signs and symptoms manifested by patients while providing a sound foundation for rational clinical care and therapy.”

“The four aspects of the disease process that form the core of pathology are its cause (etiology), the mechanisms of its development (pathogenesis), the structural alterations induced in the cells and organs of the body (morphologic changes), and the functional consequences of the morphological changes (clinical significance).”

“The nature of the morphologic changes and their distribution in different organs or tissues influence normal function and determine the clinical features (symptoms and signs), course, and prognosis of the disease.”

Id. at p. 4 (emphasis added)

Using their knowledge of clinical medicine, normal anatomy, histology and pathology, pathologists complete the sequence described by Robbins and Cotran: etiology-pathogenesis-morphological changes-clinical implications. (Ex. I, para 3). The principle of diagnostic pathology practice is to detect and interpret deviations from the established ranges of normal findings. In routine diagnostic practice, pathologists use their knowledge of normal histology as a control. The fields of anatomy and pathology have been studying these ranges of normal and abnormal appearances for over two centuries, and this knowledge is learned by pathologists during their training. (Ex A. at 5; Ex. I, para 4).

Clinical implications of morphological changes have been also studied, and the pathologists use this knowledge to provide clinically relevant information. For example, when a biopsy of a “lesion” is received by a pathologist, first he/she needs to obtain basic clinical information (site, symptoms etc.). (Ex. I at 5.) Then the specimen is examined aiming to first answer the question, “What is different from an expected normal range?” If an abnormality is present, then the main question for the pathologist is: “Is it malignant or benign?” because this will define the immediate clinical management. Then the pathologist assesses further details to

provide clinically relevant information or to answer specific questions. (*Id.*). During this process there are no samples of asymptomatic *control* individuals or “samples” used to compare to the subject sample. That is simply not how pathologists in the field practice. (*Id.* at 6.) So, if a surgeon removes tumorous tissue and sends it to the hospital pathologist to determine whether the tumor is malignant (cancerous), the pathologist does not compare that patient’s slides with slides of tissue from a non-cancerous patient. The pathologist draws upon his training, experience, and review of hundreds or thousands of other tissue analysis to diagnose a malignancy in the subject slide. (*Id.* at 7.) Likewise, as a pathologist employing the methodology used in his lab and virtually every other pathology lab at accredited institutions, Dr. Iakovlev does not require “healthy” tissue from a mesh patient without pain in order to arrive at a differential diagnosis of pain in the patient’s slides that he is analyzing. He draws upon his training, skill, and experience to apply the sequence of etiology-pathogenesis-morphological changes-clinical implications, as any pathologist would in his field of practice. *Id.*

Changes in the mesh specimens represent non-specific responses of the body to a foreign object. The first studies and descriptions of these changes date to the 1800s. (Ex. A at 5, 127, 130.) The foreign body reaction, scarring, innervation within scarred tissue, and other changes triggered by the mesh devices are well-established phenomena with established clinical implications. (Ex. A at 5-9.)

In his case-specific expert reports, Dr. Iakovlev interprets the microscopic findings as he does in his routine practice—he determines how the excised tissue is different from an appearance that he would expect to see in unaffected (normal) tissue. (Ex. I, para 5) In each specimen analysis, he specifically states that he rules out natural diseases such as tumors and foreign bodies other than the mesh. Then, he describes pathological changes triggered by the

mesh and correlates them with the clinical history. He does not use, nor does he or any other pathologist need to use, *tissue controls* or a group of asymptomatic individuals' healthy tissue to determine what the pathological changes are. (Ex. I para 6 and 7)

Simply put, requiring Dr. Iakovlev to use tissue from a patient without complications to compare it to tissue from a patient with mesh-related complications in order for him to render opinions as to whether the morphological changes seen in the slides represents a clinical correlation with the patient's symptoms is imposing a methodology that is neither required nor practiced in the field of pathology. Federal Courts in this country agree that an expert's opinion is admissible under Daubert where the expert employs the same methodology in litigation that the expert applies in practice. *See Kumho Tire*, 526 U.S. at 152; *see also Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 200 (4th Cir. 2001) (quoting *Kumho Tire* and stating that "the objective of *Daubert*'s gatekeeping requirement is to "make certain that an expert ... employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field."); *cf. Eghnayem v. Boston Sci. Corp.*, 57 F. Supp. 3d 658, 675 (S.D. W. Va. 2014) ("So long as an expert 'employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field,' he does not necessarily have to perform a physical examination of the patient to offer an expert opinion.").

For these reasons, Ethicon's motion to exclude Dr. Iakovlev's opinions regarding complications in the slides that he analyzes by applying well-accepted methodologies in the field of pathology should be denied.

III. CONCLUSION

For the reasons stated herein, Plaintiffs respectfully request that the Court DENY the defendants' Motion to Exclude the Testimony of Dr. Iakovlev in its entirety.

Dated: October 11, 2016

Respectfully submitted,

/s/ Benjamin H. Anderson

Benjamin H. Anderson, Esq.
Anderson Law Offices, LLC
17138 Lorain Avenue, Suite 211
Cleveland, Ohio 44111
216-589-0256
E-mail: ben@andersonlawoffices.net

CERTIFICATE OF SERVICE

I hereby certify that on October 11, 2016, I electronically filed the foregoing document with the Clerk of the court using CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL.

/s/ Benjamin H. Anderson
Benjamin H. Anderson, Esq.
Anderson Law Offices, LLC
17138 Lorain Avenue, Suite 211
Cleveland, Ohio 44111
(216) 589-0256
(216) 916-0988 (fax)
E-mail: ben@andersonlawoffices.net